



RESEARCH FACILITIES

## Little Castle on the Prairie

Can \$400 million and a “Manhattan Project for diabetes” transform South Dakota into a research hub?

The flagship building for Sanford Health in Sioux Falls, South Dakota, really does fly flags, colored pennants over ramparts and turrets. Shields with pseudoheraldic symbols hang inside, and wooden thrones overlook the lobby. This children’s hospital runs on what it calls the “Disney principle”: Just as children never see the Mickey Mouse mascot at Disneyland without his head on, Sanford never lets the fantasy lapse with a bare surface. CT scanners have twisting otters painted on them, and doors of tiny, Wonderland size appear in the hallway, opening onto dioramas of secret worlds. Had Alice fallen ill, she would have convalesced at something like the Sanford Castle.

With so much invested in decoration, the castle is decidedly a patients’ hospital. Indeed, the focus of Sanford Health (a cluster of clinics formerly known as Sioux Valley Hospital and Health) has always been patient care, not clinical science. But recently, the institution’s stepsister of a research arm was transformed. T. Denny Sanford, a banking mogul, had already donated \$16 million to build the castle in 2004, an astounding amount for South Dakota. To help push beyond caring for patients, in February 2007 Sanford donated \$400 million more, largely for medical research—one of the largest gifts ever bestowed on any U.S. hospital. Rich Adcock, an executive vice president at Sanford, said the hospital had a vision for growth, “but we knew we needed an angel. Denny Sanford was that angel.”

With Sanford’s blessing, officials announced what’s known as the Sanford Project: a plan to cure one widespread disease within Sanford’s lifetime. The deadline is a challenge; Sanford turns 75 this year. After interviewing experts, project directors selected type 1 diabetes (juvenile diabetes), a disorder in which immune cells destroy the body’s beta cells, the insulin-secreting cells in the pancreas. Newt Gingrich, the former U.S. House of Representatives speaker and a health care–reform advocate, showed up to help announce what Sanford Health is calling a “Manhattan Project.”

Conquering diabetes is ambitious enough, but then the project declared it had already settled on the approach it would take: harnessing the body’s ability to regenerate beta cells. The choice startled some diabetes scientists who saw equal or more promise in other approaches—stem-cell therapy or beta-cell transplants. And the ultimate goal of the Sanford Project may be even more audacious: enticing enough scientific talent to create a permanent biomedical hub, a Boston or San Diego, in the 46th most populous state in the union.

### ‘Let’s start tomorrow’

Paul Burn, a biochemist and head of research for the Sanford Project, is exasperated that most clinical diabetes research focuses on preventing overactive immune cells from destroying beta cells. Doctors normally don’t diagnose children with dia-

**Night lights.** Sanford Health plans to build about 20 children’s clinics worldwide, all shaped like castles.

betes until they’ve lost 90% of their beta cells, so corralling their immune systems alone won’t reverse the damage, he argues. He thinks it’s essential to regenerate healthy beta cells to cure the disease.

But if Burn merely wanted to realign research priorities, he could have stayed at his old job as vice president of research for the Juvenile Diabetes Research Foundation (JDRF) in New York City. He came to Sioux Falls to run a different kind of clinic, one that, he says, “is making big bets.” His team won’t be doing basic research, though: “Our focus will really be on proof-of-concept studies,” including clinical trials.

Burn sees a gap between research and drug development for type 1 diabetes and wants Sanford to bridge it. Based on the years he worked for drug companies, Burn argues that they have little financial incentive to run trials for type 1 diabetes when there’s a larger and far more lucrative market for the distinct problem of adult-onset, or type 2, diabetes. (Burn estimates that 90% of research dollars spent on diabetes fund type 2 work.) “Even beyond 2015, there’s no cure in the pipeline” for type 1, Burn says. “It’s the same old story of trying to deliver insulin in a new way.”

Because Sanford does little basic research, Burn hopes that places like the Diabetes Center of Excellence at the University of Florida, Gainesville, or the Burnham Institute based in San Diego (and the recipient of its own \$30 million gift from Sanford), will funnel promising lab results to him for clinical trials. Burn drew on his JDRF contacts to set up these partnerships, but the ties are loose, and no one will coordinate the direction of basic research among the clinics.

Burn is now interviewing for six positions to run clinical trials at Sanford, and he already has his core research team in place. The project impressed many doubters in June 2009 by unveiling a surprisingly international group, including scientists from China and Russia. (Burn, who is Swiss, has a Ph.D. from the University of Basel.) One early recruit was Alexander Rabinovitch, a gaunt Canadian forced into retirement because of his age by the University of Alberta in Edmonton. His lab in Canada had significantly boosted the numbers of beta cells in mice by using two drugs already approved by the Food and Drug Administration for other purposes, and he was eager to expand into human trials. No one seemed likely to sponsor the work, however. When Burn heard this, he immediately

dipped into the \$400 million and offered to fund it. It will start this March or April, the first trial initiated at Sanford.

It's an example of the flexibility that nine figures can buy. Sanford Health—which partners with the University of South Dakota School of Medicine—maintains that its annual research budget for diabetes will approach \$100 million per year. Burn hopes his scientists can win grants to cover much of that, but he can also cut through bureaucratic tape himself. “If they have a good project, I tell them, ‘Here’s the money, let’s start tomorrow.’”

Burn sees advantages even in the remoteness of Sioux Falls. With a dearth of competition from other research clinics, Sanford will have its pick of diabetes patients from the nearby population of 155,000. Sioux Falls does not support a deep scientific community like larger cities do, he admits, “but it’s a paradise from the point of view of trying to set up a clinical trial.” What’s more, Sanford Castle is just the first of 20-some castles planned. Another one financed by Sanford opened in August in Oklahoma, and administrators are scouting sites in Belize, Ireland, and elsewhere. Burn hopes to recruit diabetes patients through each castle.

### Creeping doubts

Not everyone imagines a research utopia in Sioux Falls. “I think some people really share my concern that it’s not an established scientific community,” says Gordon Weir, a Harvard University molecular biologist who works on regenerating beta cells.

Hendrik-Jan Schuurman, a diabetes researcher at the University of Minnesota, Twin Cities, is more supportive but echoes Weir’s concerns: “Everybody knows the university in South Dakota is not an institute with a reputation for biomedical research.” That’s why he thought Sanford was prudent to establish ties with Burnham and the Florida diabetes center, places that can provide support and advice for Sanford while it builds up the long-term research infrastructure it will need.

Scientists have also questioned putting so much money into just one option—beta-cell regeneration—when other ideas seem worth trying. Schuurman and colleagues in New Zealand have developed ways to transplant pig pancreatic cells into patients, by coating the cells to enable them to escape detection by the immune system. Schuurman acknowledges



**Big bets.** Paul Burn wants to cure type 1 diabetes and build a research hub in Sioux Falls.

that pig cells are not a long-term solution—the donor pigs must be raised in supersterile bays at costs of \$50 per day per pig—but feels they are the best short-term hope (*Science*, 20 November 2009, p. 1049).

Weir touts regenerating beta cells from embryonic stem cells or induced pluripotent stem cells (iPS cells): adult cells that have been reprogrammed to a stemlike state. Adult cells present challenges, such as the need to remove epigenetic imprinting, Weir says, “and we’re still figuring out whether there are [other] differences that would not allow them to succeed.” For these reasons, he feels that generating beta cells from embryonic stem cells (ES) is the most attractive path.

Burn argues that stem-cell therapies, adult or embryonic, are 20 or 30 years distant, and he’s impatient. Yet there’s another reason Sanford will not sponsor embryonic stem cell work: South Dakota has banned it. A local advocacy group, South Dakotans for Lifesaving Cures, calls the ban the most

restrictive in the country, as it might prohibit citizens from receiving ES treatments developed elsewhere. The group plans to introduce a bill into the state legislature to lift the ban, partly to aid research, says spokesperson Nathan Peterson: “We have top-notch medical facilities, and there isn’t any reason the scientists shouldn’t have the option of conducting [ES] work in an ethical manner.” Sanford, however, refuses to take a public stand on lifting the ES ban.

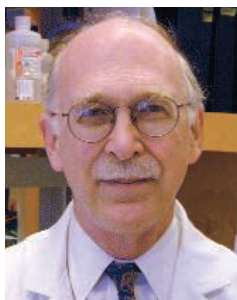
### Room to grow

While the Sanford Project still publicly proclaims it will oversee \$100 million of research a year and cure diabetes through beta-cell regeneration alone, in private Burn backs off a bit. The project will spend about \$30 million in 2010, and he diplomatically calls \$100 million an “ambitious” number. He also says Sanford will explore areas beyond regeneration, perhaps dabbling in iPS or even immunological work.

At the same time, Burn isn’t shying away from the Sanford Project’s vow to cure type 1 diabetes, soon. He’s overseeing a move into a new headquarters, a 28,000-m<sup>2</sup> building on the outskirts of Sioux Falls. Burn hopes to move 150 people into one of its two 5,600-m<sup>2</sup> research bays by this summer and fill a second bay later. “At universities, you’re often fighting over every square foot,” Burn notes from a snowy and truly capacious parking lot. “Here space should be no issue.”

As for the future, Sanford Health plans to open a 75-hectare research campus south of town and keep the momentum of the Sanford Project going after it cures type 1 diabetes. Burn believes beta-cell regeneration holds great promise for curing type 2 as well. Indeed, Burn sees no reason Sanford can’t build a green oasis of research in an otherwise barren scientific state. And even skeptics of the project admit that \$400 million is a lot of green. “You can create a scientific environment in even Timbuktu,” says Harvard’s Weir. “If you make it big enough and get enough people there, you can succeed.”

—SAM KEAN



**Doubts.** Harvard’s Gordon Weir and others ask if the project can succeed.